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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/667,328	09/21/2000	Gary W. Pace	121-112	8438

7590 10/16/2002

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EXAMINER
GOLLAMUDI, SHARMILA S

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 10/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/667,328	PACE ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Receipt of Extension of Time and Amendment B received on July 12, 2002 are acknowledged. Claims 16-38 are included in the prosecution of this application.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Rejection of claims 16-18, 20-32, and 34-38 under 35 U.S.C. 102(a) as being anticipated by WO 99/29316 is maintained.

Response to Arguments

Applicant argues that Severson et al fails to disclose a non-aqueous hydrophobic liquid in which said biologically active substance is not soluble or poorly soluble. Secondly, applicant argues that Severson et al discloses a composition containing an omega-3 fatty acid and a therapeutic agent that is substantially soluble in the omega-3 fatty acid. Lastly, it is argued that the reference teaches the particles dissolved the medium, therefore it cannot disclose the instant particle size.

Applicant's arguments have been fully considered but they are not persuasive. Severson discloses water-insoluble therapeutic agents; i.e. fenofibrate and cyclosporin, a carrier medium containing a hydrophobic component, i.e. omega-3 fatty acid and

surfactant system, i.e. TWEEN 80 and Myrj 52. The composition contains less than 10% of the hydrophilic substance. The examiner points out that applicant's arguments are contradicting instant invention and claims. Applicant argues that fenofibrate and cyclosporin are solubilized in the carrier medium (hydrophobic liquid). Applicant is correct in that cyclosporin is lipid soluble as noted on page 2 of Severson and water-insoluble. However, the examiner points out that applicant's specification and dependent claims recite omega 3-fatty acid as part of the Markush group for the hydrophobic component. Further, the instant specification and dependent claims recite cyclosporin and fenofibrate as the active agent. This argument is directly contradicting the instant invention. Additionally, the examiner points out Table 1 on page 26 of instant specification in which the oil phase contains cyclosporin and fatty acid ester as seen in Severson. The examiner fails to see the difference between the instant specification and the prior art. Also, the applicant has not recited any specific amounts to differentiate the instant invention from the prior art and to substantiate how the applicant's active is insoluble in lipid when the state of art clearly teaches its solubility. Secondly, the preconcentrate is then dispersed in an aqueous solution to form a dispersion as seen in instant claims (Note claim 17). Lastly, the examiner points to page 34 in which the particle size of the microemulsion when diluted with water. The examiner points to formulation 19 for the particle size of the active.

Therefore, Severson et al anticipates the instant invention and the rejection is maintained.

Rejection of claims 16-18, 20-32, and 34-38 under 35 U.S.C. 102(a) as being anticipated by WO 99/29300 is maintained.

Response to Arguments

Applicant argues that RTP Pharma teaches a composition containing fenofibrate solubilized in a carrier media and the references fails to disclose a non-aqueous hydrophobic liquid in which said biologically active substance is not soluble or poorly soluble. It is argued that RTP Pharma does not disclose solid particles of the water-insoluble drug.

Applicant's arguments have been fully considered but they are not persuasive. The hydrophobic components included triglycerides, fish oils, free fatty acids and esters, etcetera. The surfactant is a non-surfactant, i.e. polyoxyethylene-sorbitan-fatty acid ester (pg. 7). The instant claims require a water-insoluble active and RTP Pharma discloses that fenofibrate is insoluble in water on page 2, which independent claim requires. Applicant is correct that fenofibrate is solubilized in the carrier hydrophobic carrier medium. However, the examiner points out that the actives that are to be dispersed in the hydrophobic liquid recite fenofibrate in depending claim 23 and instant specification's fenofibrate composition on page 26. Applicant's arguments are contradicting the instant invention and claims as addressed above. Again the examiner points out that the applicant has not recited any specific amounts to differentiate the instant invention from the prior art and to substantiate how the applicant's active is insoluble in lipid when the state of art clearly teaches its solubility. Lastly, the particle

size of the preconcentrate when dispersed in an aqueous media is on the average of 5 microns or less (Note claim 9).

Therefore, RTP Pharma anticipates the instant invention and the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Rejection of claims 16-27 and 30-38 under 35 U.S.C. 103(a) as being unpatentable over Parikh et al (5660858) in view Haynes (5091187) is maintained.

Response to Arguments

Applicant argues that there is no motivation the two references. Applicant argues that Parikh teaches cyclosporin dissolved in a medium chain trigylceride whereas the instant invention teaches solid particles of a biologically active substance in a hydrophobic liquid. It is argued that the reference teaches not only dissolving the cyclosporin in the oil phase, but also teaches adding it to an aqueous solution and homogenizing it to form an emulsion. Applicant argues that Haynes teaches away from the instant invention since Haynes does not teach a hydrophobic liquid.

Applicant's arguments have been fully considered but they are not persuasive. As addressed above, the argument that cyclosporin of the prior art dissolves in the

hydrophobic liquid, contradicts the instant invention and dependent claims. As noted by Severson et al, cyclosporin is soluble in lipids. Instant specification provides an example combining cyclosporin and free fatty acid esters. The assertion that the cyclosporin is not dissolved in the oil phase when the prior art teaches it does and since the prior art uses the instant lipids in depending claims, is not understood. Secondly, Parikh teaches homogenizing the oil solution with an aqueous solution to form droplets, specifically volume weighted mean particle sizes (note column 5). The examiner also points out that this particle size reads on instant particle range. Additionally, as noted by the applicant, the oil solution is homogenized to form an *emulsion.* Grant and Hackh's Chemical Dictionary (attached) defines an emulsion as a fluid consisting of a microscopically heterogeneous mixture of 2 immiscible liquid phases, in which one liquid forms minute droplets suspended in the other. Therefore, the prior art reads on instant invention's suspension of oil droplets containing the active in an aqueous medium. In regards to the motivation to combine, the examiner points out that Parikh teaches emulsions to be used parenterally on column 2, lines 45. Haynes is relied upon to teach instant droplet sizes for injections. Haynes teaches the instant size in order to prevent blocking of the arteries. Haynes is used as a secondary reference and its specific teachings. The primary reference teaches the broad teaching of the composition. One of ordinary skill would look to Haynes to teach particle sizes that are conducive to parenteral administration.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is (703) 305-2147. The examiner can be normally reached M-F from 7:30 am to 4:15pm.

If attempts to reach the examiner by the telephone are unsuccessful, the examiner's supervisor, Jose Dees, can be reached at (703) 308-4628. The fax number for this organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist, whose telephone number is (703) 308-1235.

SSG

October 9, 2002

JOSE' G. DEES
SUPERVISORY PATENT EXAMINER

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